DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Peter Parsonson
Associate Director, Regulatory Affairs
Alcon Research, Ltd.
6201 South Freeway R3-54
Fort Worth, TX 76134-2099

RE: NDA # 021545
PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2%
MA # 272

Dear Mr. Parsonson:

As part of its routine monitoring and surveillance program, the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a Patient Education Brochure (PAT12057PA) (brochure) for PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% (Pataday) submitted by Alcon Research, Ltd. (Alcon) under cover of Form FDA-2253. The promotional material is false or misleading because it omits material facts, makes unsubstantiated efficacy claims, overstates the efficacy, and makes unsubstantiated superiority claims for the drug. Therefore, the brochure misbrands Pataday in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 352(a) & 321(n), and implementing regulation 21 CFR 1.21(a). *Cf.* 21 CFR 202.1(e)(5)(i), (iii); (e)(6)(ii); (e)(7)(i), (iii).

Background

Below is the indication and summary of the most serious and most common risks associated with the use of Pataday.[1]

Pataday is indicated for the treatment of ocular itching associated with allergic conjunctivitis. The FDA-approved product labeling (PI) for Pataday includes Warnings and Precautions regarding topical use only, contamination of tip and solution, and contact lens use. In addition, symptoms similar to cold syndrome and pharyngitis were reported at an incidence of approximately 10% with Pataday use.

[1] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

Omission of Material Fact

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. Page four of the brochure includes the following claims (emphasis original):

- "**Can I use PATADAY™ Solution if I wear contact lenses?**

  Talk to your eye care professional about using PATADAY™ Solution with contact lenses. Don't wear contact lenses if your eyes are red. PATADAY™ Solution should not be used to treat contact lens-related irritation. Always remove your contact lenses before administering PATADAY Solution."

This presentation misleadingly omits material facts regarding the Warning and Precaution instructing patients to wait ten minutes after using Pataday before inserting soft contact lenses. According to the PI, "[p]atients who wear soft contact lenses and **whose eyes are not red**, should be instructed to wait at least ten minutes after instilling PATADAY™ olopatadine hydrochloride ophthalmic solution) 0.2% before they insert their contact lenses." (emphasis original) We acknowledge that page six of the brochure includes this information; however, failure to include this important material risk information in a section of the brochure dedicated to the use of Pataday while wearing contact lenses is misleading.

Unsubstantiated Efficacy Claims

Promotional materials are misleading if they represent or suggest that a drug is more effective than has been demonstrated by substantial evidence or substantial clinical experience. Page two of the brochure includes the following claims: (emphasis original)

> "**It is important to identify and treat your allergy eye symptoms because** (citation omitted):
>
> **1** They can be uncomfortable
>
> **2** They can lead to eye damage, due to excessive scratching or rubbing
>
> **3** They can impact your overall eye health"

These claims misleadingly suggest that Pataday has demonstrated efficacy in treating all "allergy eye symptoms," improves "overall eye health," prevents "eye damage," and can positively impact eye comfort when this is not the case. Pataday is only approved for the treatment of "**ocular itching** associated with allergic conjunctivitis," and there is no substantial evidence or substantial clinical experience demonstrating that Pataday had any clinically meaningful reductions in other signs and symptoms associated with allergic conjunctivitis other than itching such as conjunctival redness, tearing, chemosis, and eyelid swelling. (emphasis added) Therefore, claims that imply that Pataday is effective in treating all "allergy eye symptoms," improving "overall eye health," preventing "eye damage," and

positively impacting eye comfort are misleading.

Overstatement of Efficacy

Promotional materials are misleading if they represent or suggest that a drug is more effective or safer than has been demonstrated by substantial evidence or substantial clinical experience. The brochure includes the following claims (emphasis original):

- "With one drop daily of PATADAY™ Solution, you can start and finish the day with zero-itch."[2] (page 3)
- "PATADAY™ Solution stops the itching . . ." (page 3)
- "You'll be free to go about your normal activities and not give those itchy allergy eyes a second thought." (page 4)
- **"Zero-itch** within minutes and up to 16 hours later with just **one drop** daily."[2] (page 5)
- "**What is the difference between minimal and zero-itch?**
  Different eye allergy medicines have different levels of effectiveness. Many only minimize itch, but PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% eliminates it (zero-itch). Clinical studies have shown that one drop of PATADAY™ Solution provides zero-itch at 3 minutes and lasts up to16 hours." [2] (page 5)

These claims are misleading because they suggest that **all** patients who use Pataday will experience "zero-itch" and be symptom-free (i.e., "not give those itchy eyes a second thought") when this was not demonstrated by substantial evidence or substantial clinical experience. Specifically, the cited reference, a post-hoc analysis discussed in a poster presentation, does not constitute substantial evidence or substantial clinical experience that would support such a claim. In addition, the clinical trials submitted for the approval of Pataday demonstrated that only 30 to 60 percent of patients treated with Pataday experienced complete relief of their ocular itching at the pre-specified time points.

Unsubstantiated Superiority

Promotional materials are misleading if they represent or suggest that a drug is safer or more effective than another drug, when this has not been demonstrated by substantial evidence or substantial clinical experience. Page five of the brochure includes the following claim:

- "**What is the difference between minimal and zero-itch?**
  Different eye allergy medicines have different levels of effectiveness. Many only minimize itch, but PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% eliminates it (zero-itch)."[2]

These claims misleadingly suggest that Pataday provides superior relief by providing all patients with "zero-itch," as compared to other available therapies approved for the treatment of ocular allergies which only "minimize" ocular itching. Such claims of superiority must be supported by adequate and well-controlled head-to-head clinical trials comparing appropriate doses and dose regimens of your drug and the comparator drug or drugs. The cited

[2]Blaiss MS, Tort MJ. Zero itch in eyes treated with olopatadine hydrochloride ophthalmic solution, 0.2% in bilateral conjunctival allergen challenge studies. Poster presented at: World Allergy Conference; December 2011; Cancun, Mexico.

reference was a post-hoc analysis with a placebo vehicle as the comparator, discussed in a poster presentation, and therefore does not constitute substantial evidence or substantial clinical experience that would support these claims. OPDP is not aware of substantial evidence or substantial clinical experience to support any suggestion that Pataday demonstrates superior efficacy over other products indicated for ocular itching associated with allergic conjunctivitis. If you have data to support these claims, please submit them to FDA for review.

Conclusion and Requested Action

For the reasons discussed above, the brochure misbrands Pataday in violation of the FD&C Act, 21 U.S.C. 352(a) & 321(n), and implementing regulation 21 CFR 1.21(a). *Cf.* 21 CFR 202.1(e)(5)(i), (iii); (e)(6)(ii); (e)(7)(i), (iii).

OPDP requests that Alcon immediately cease the dissemination of violative promotional materials for Pataday such as those described above. Please submit a written response to this letter on or before February 20, 2013, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Pataday that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, Division of Consumer Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266** or by facsimile at (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA # 272 in addition to the NDA number in all future correspondence relating to this particular matter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Pataday comply with each applicable requirement of the FD&C Act.

Sincerely,

{See appended electronic signature page}

Adora Ndu, Pharm.D.
LCDR, USPHS
Regulatory Review Officer
Division of Consumer Drug Promotion
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Amy Toscano, Pharm.D., RAC, CPA
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/s/

ADORA NDU
02/05/2013

AMY TOSCANO
02/05/2013